```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:ssspta1653hxp

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  MAY 01   New CAS web site launched
 NEWS  3  MAY 08   CA/CAplus Indian patent publication number format defined
 NEWS  4  MAY 14   RDISCLOSURE on STN Easy enhanced with new search and display
                   fields
 NEWS  5  MAY 21   BIOSIS reloaded and enhanced with archival data
 NEWS  6  MAY 21   TOXCENTER enhanced with BIOSIS reload
 NEWS  7  MAY 21   CA/CAplus enhanced with additional kind codes for German
                   patents
 NEWS  8  MAY 22   CA/CAplus enhanced with IPC reclassification in Japanese
                   patents
 NEWS  9  JUN 27   CA/CAplus enhanced with pre-1967 CAS Registry Numbers
 NEWS 10  JUN 29   STN Viewer now available
 NEWS 11  JUN 29   STN Express, Version 8.2, now available
 NEWS 12  JUL 02   LEMBASE coverage updated
 NEWS 13  JUL 02   LMEDLINE coverage updated
 NEWS 14  JUL 02   SCISEARCH enhanced with complete author names
 NEWS 15  JUL 02   CHEMCATS accession numbers revised
 NEWS 16  JUL 02   CA/CAplus enhanced with utility model patents from China
 NEWS 17  JUL 16   CAplus enhanced with French and German abstracts
 NEWS 18  JUL 18   CA/CAplus patent coverage enhanced
 NEWS 19  JUL 26   USPATFULL/USPAT2 enhanced with IPC reclassification
 NEWS 20  JUL 30   USGENE now available on STN
 NEWS 21  AUG 06   CAS REGISTRY enhanced with new experimental property tags
 NEWS 22  AUG 06   BEILSTEIN updated with new compounds
 NEWS 23  AUG 06   FSTA enhanced with new thesaurus edition

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:36:13 ON 06 AUG 2007
```

```
=> file medline
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 17:36:28 ON 06 AUG 2007

 FILE LAST UPDATED: 5 Aug 2007 (20070805/UP).  FILE COVERS 1950 TO DATE.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s ang-1 protein
         8612 ANG
      4050850 1
      1691132 PROTEIN
L1          14 ANG-1 PROTEIN
               (ANG(W)1(W)PROTEIN)

=> d l1 ti abs ibib tot

L1   ANSWER 1 OF 14     MEDLINE on STN
TI   Parathyroid hormone (1-34) augments angiopoietin-1 expression in human
     osteoblast-like cells.
AB   Parathyroid hormone (PTH) is a major regulatory factor in skeletal
     physiology.  However, the molecular mechanism underlying the effects of
     PTH on bones has yet to be elucidated in detail.  Recently, some reports
     have demonstrated the crucial role of bone vasculature with regard to bone
     density.  Angiopoietin-1 (Ang-1), along with VEGF, has been established as
     a primary angiogenic regulatory agent.  In this study, we have attempted
     to characterize the effects of PTH (1-34) on Ang-1 expression and
     signaling molecules, employing primary-cultured human osteoblast-like
     cells.  Quiescent osteoblasts were exposed to PTH (1-34), after which
     Ang-1 expression was determined at the mRNA and protein levels.  Reverse
     transcription-polymerase chain reaction (RT-PCR) analyses indicated that
     Ang-1 mRNA expression increased as the result of PTH (1-34) treatment.
     The expression of the Ang-1 protein was also
     augmented as the result of treatment with PTH (1-34).  An adenylyl cyclase
     activator, forskolin, was shown to induce Ang-1 mRNA expression, whereas
     the protein kinase A inhibitor, H-89, blocked the PTH (1-34)-mediated
     expression of Ang-1 mRNA.  These findings indicate that PTH
     (1-34)-mediated Ang-1 expression involves adenylyl cyclase-protein kinase
     A dependent signaling.  Our observations also show that Ang-1 may perform
     a crucial role in the effects of PTH (1-34) on bones, possibly involving
     alterations in bone vasculature.
ACCESSION NUMBER:    2006606096      MEDLINE
DOCUMENT NUMBER:     PubMed ID: 17039426
TITLE:               Parathyroid hormone (1-34) augments angiopoietin-1
                     expression in human osteoblast-like cells.
AUTHOR:              Park J H; Song H I; Rho J M; Kim M R; Kim J R; Park B H;
                     Park T S; Baek H S
CORPORATE SOURCE:    Division of Endocrinology and Metabolism, Department of
                     Internal Medicine, Chonbuk National University Medical
                     School, Jeonju, Republic of Korea.. parkjh@chonbuk.ac.kr
SOURCE:              Experimental and clinical endocrinology & diabetes :
                     official journal, German Society of Endocrinology [and]
                     German Diabetes Association, (2006 Sep) Vol. 114, No. 8,
                     pp. 438-43.
                     Journal code: 9505926. ISSN: 0947-7349.
PUB. COUNTRY:        Germany: Germany, Federal Republic of
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
```

ENTRY MONTH: 200611
ENTRY DATE: Entered STN: 14 Oct 2006
Last Updated on STN: 15 Nov 2006
Entered Medline: 14 Nov 2006

L1 ANSWER 2 OF 14 MEDLINE on STN
TI Sildenafil induces angiogenic response in human coronary arteriolar endothelial cells through the expression of thioredoxin, hemeoxygenase and vascular endothelial growth factor.
AB This study was undertaken to investigate the effect of phosphodiesterase-5 (PDE5) inhibitor, sildenafil, on angiogenic response in human coronary arteriolar endothelial cells (HCAEC). The cells exposed to sildenafil (1-20 microM) demonstrated significantly accelerated tubular morphogenesis with the induction of thioredoxin-1 (Trx-1), hemeoxygenase-1 (HO-1) and VEGF. Sildenafil induced VEGF and angiopoietin specific receptors such as KDR, Tie-1 and Tie-2. This angiogenic response was repressed by tinprotoporphyrin IX (SnPP), an inhibitor of HO-1 enzyme activity. Sildenafil below 1 muM has no angiogenic effect as evidenced by reduced tuborogenesis. Sildenafil along with SnPP inhibited both VEGF and Angiopoietin-1 (Ang-1) protein expression.
Therefore our results demonstrated for the first time that sildenafil is a very potent pro-angiogenic factor.
ACCESSION NUMBER: 2006555561 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16716755
TITLE: Sildenafil induces angiogenic response in human coronary arteriolar endothelial cells through the expression of thioredoxin, hemeoxygenase and vascular endothelial growth factor.
AUTHOR: Vidavalur Ramesh; Penumathsa Suresh Varma; Zhan Lijun; Thirunavukkarasu Mahesh; Maulik Nilanjana
CORPORATE SOURCE: Department of Pediatrics, University of Connecticut Health Center, Farmington, CT 06030-1110, USA.
CONTRACT NUMBER: HL 56803 (NHLBI)
HL 69910 (NHLBI)
SOURCE: Vascular pharmacology, (2006 Aug) Vol. 45, No. 2, pp. 91-5.
Electronic Publication: 2006-05-22.
Journal code: 101130615. ISSN: 1537-1891.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200702
ENTRY DATE: Entered STN: 19 Sep 2006
Last Updated on STN: 10 Feb 2007
Entered Medline: 9 Feb 2007

L1 ANSWER 3 OF 14 MEDLINE on STN
TI Correlation between the expression of angiopoietins and their receptor and angiogenesis in gastric cancers.
AB OBJECTIVE: To explore the effects of angiopoietins (Ang-1 and Ang-2) and Tie-2 expression on microvessel density (MVD) in gastric cancers. METHODS: By using semiquantitative RT-PCR, immunohistochemistry and image analysis system, the expression of Ang-1, Ang-2, Tie-2 mRNA and their proteins were detected in 68 primary gastric cancers and their adjacent normal tissues. Microvessel density (MVD) was figured out based on CD34 immunohistochemical staining. RESULTS: The expression of all Ang-1, Ang -2, Tie-2 mRNA and their proteins was detected in gastric cancers and their paired adjacent gastric mucosa tissues. A negative correlation between Ang-1 protein, Tie-2 mRNA and MVD in gastric cancers was observed ($r = -0.440$, $r = -0.267$; $P < 0.05$), while the relation between Ang-2 mRNA and its protein, Ang-2/Ang-1 protein ratio with MVD were positive ($r = 0.319$, $r = 0.729$, $r = 0.739$; $P < 0.05$). It was found that MVD in groups with Ang-2 mRNA T/N

ratio over 1.2 (the ratio of Ang-2 mRNA in gastric cancers and its adjacent normal mucosa) was higher than that in those with a ratio under 1.2, revealed by analysing the effects of Ang-1 and Ang-2 mRNA T/N ratio on MVD in gastric cancers. CONCLUSION: Ang-1 activates Tie-2 receptor, whereas Ang-2 antagonizes Ang-1 in the angiogenesis, and the Ang-2/Ang-1 ratio determines angiogenesis and tumor growth in gastric cancers. When the expression of Ang-2 is high and Ang-1 is low, the angiogenesis in gastric cancers is promoted, otherwise oppositely. The role of Ang-2 is dominant in the effect of Angs and their receptor on angiogenesis in gastric cancers.

ACCESSION NUMBER: 2006454777 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16875629
TITLE: Correlation between the expression of angiopoietins and their receptor and angiogenesis in gastric cancers.
AUTHOR: Zhang Zhen-zhen; Zhang Sheng; Lin Jian-yin; Huang Pei-sheng; Chen Yu-peng
CORPORATE SOURCE: Department of Pathology, The First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, China.
SOURCE: Zhonghua zhong liu za zhi [Chinese journal of oncology], (2006 Apr) Vol. 28, No. 4, pp. 280-4.
Journal code: 7910681. ISSN: 0253-3766.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 1 Aug 2006
Last Updated on STN: 12 Dec 2006

L1 ANSWER 4 OF 14 MEDLINE on STN
TI Angiotensin type 1 receptor blocker restores podocyte potential to promote glomerular endothelial cell growth.
AB Both podocytes and glomerular endothelial cells (GEN) are postulated to play important roles in the progression and potential regression of glomerulosclerosis. Inhibition of angiotensin is crucial in treatment of chronic kidney disease, presumably via effects on BP and extracellular matrix. This study aimed to investigate how angiotensin inhibition altered the interactions between podocytes and GEN. The effects of supernatants from primary cultured mouse podocytes, before or after sublethal injury by puromycin aminonucleoside, in the presence or absence of angiotensin type 1 receptor blocker (ARB), on GEN sprouting and growth were assessed. Supernatant from normal podocytes significantly increased GEN sprouting, whereas puromycin aminonucleoside-injured podocyte supernatant decreased these GEN responses. These effects were linked to decreased vascular endothelial growth factor A (VEGF-A) and angiopoietin-1 (Ang-1) protein from injured podocytes.
This downregulation of VEGF-A and Ang-1
protein was reversed when injured podocytes were treated with ARB.
Inhibition of VEGF-A or Ang-1 prevented this restored response by ARB.
Activation of intracellular kinases (p38, extracellular signal-regulated kinase, and AKT) was suppressed in GEN that were treated with medium from injured podocytes but restored by medium from ARB-treated injured podocytes. Therefore, injured podocytes are ineffective in promoting GEN sprouting, and this effect is reversed by ARB treatment of the injured podocyte. These data support the idea that ARB effects on podocytes may mediate capillary remodeling in vivo.

ACCESSION NUMBER: 2006381739 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16790514
TITLE: Angiotensin type 1 receptor blocker restores podocyte potential to promote glomerular endothelial cell growth.
AUTHOR: Liang Xiu-Bin; Ma Li-Jun; Naito Takashi; Wang Yihan; Madaio Michael; Zent Roy; Pozzi Ambra; Fogo Agnes B
CORPORATE SOURCE: Department of Pathology, Vanderbilt University Medical Center, Nashville, TN 37232-2561, USA.

CONTRACT NUMBER: DK44757 (NIDDK)
DK56942 (NIDDK)
SOURCE: Journal of the American Society of Nephrology : JASN, (2006 Jul) Vol. 17, No. 7, pp. 1886-95. Electronic Publication: 2006-06-21.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 27 Jun 2006
Last Updated on STN: 31 Oct 2006
Entered Medline: 30 Oct 2006

L1 ANSWER 5 OF 14 MEDLINE on STN
TI Combined gene therapy enhances collateral vascularization in coronary artery occlusion swine model.
AB OBJECTIVE: To investigate the efficacy of combined gene transfer of vascular endothelial growth factor (VEGF) and angiotensin-1 (Ang-1) in swine coronary artery occlusion. METHODS: Swine underwent left thoracotomy followed by ligation of left anterior descending coronary artery. Constructed PCD(2)/VEGF and/or PCD(2)/Ang-1 eukaryotic expression plasmid was directly injected into the swine myocardium. RT-PCR, immunohistochemistry, capillary density and arteriole density were used to detect gene expression and biological effect. Coronary angiography was done to evaluate collateral circulation of the occluded artery. RESULTS: High levels of VEGF and Ang-1 mRNA and protein expression were detected. There was a significant increase in the number of capillaries and arterioles as compared with a control group ($P < 0.05$). Capillary density and arteriole density of the combination therapy group were higher than those of the swing receiving either therapy alone. Coronary angiography showed better collateral circulation in the combination therapy group. CONCLUSIONS: Direct injection of PCD(2)/VEGF and PCD(2)/Ang-1 can transfect the myocardium and express VEGF and Ang-1 protein. Combined gene transfer of VEGF and Ang-1 can increase capillary and arteriole number and enhance collateral circulation of the occluded coronary artery more effectively.
ACCESSION NUMBER: 2005101430 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15730732
TITLE: Combined gene therapy enhances collateral vascularization in coronary artery occlusion swine model.
AUTHOR: Zu Ling-yun; Jiang Jie; Yang Yang; Chen Ming; Chen Li; Yu Zhuo; Gao Wei
CORPORATE SOURCE: Department of Cardiology, Peking University Third Hospital, Beijing 100034, China.
SOURCE: Zhonghua nei ke za zhi [Chinese journal of internal medicine], (2004 Dec) Vol. 43, No. 12, pp. 896-9.
Journal code: 16210490R. ISSN: 0578-1426.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 1 Mar 2005
Last Updated on STN: 3 Sep 2005
Entered Medline: 2 Sep 2005

L1 ANSWER 6 OF 14 MEDLINE on STN
TI Endometrial angiopoietin expression and modulation by thrombin and steroid hormones: a mechanism for abnormal angiogenesis following long-term

progestin-only contraception.

AB The angiopoietins (Ang) are endothelial cell-related factors necessary for the development and maintenance of all vessels. Altering the expression of these proteins would be expected to result in aberrant angiogenesis. Indeed the fragile endometrial vasculature and bleeding observed in women treated with long-term progestin-only contraceptives has been associated with changes in the expression of Ang-1 and Ang-2. Since bleeding would result in thrombin formation, we have assessed the effects of thrombin on the expression of the Angs in human endometrial cells. This study shows that thrombin significantly reduces the expression of Ang-1 protein and mRNA expression in human endometrial stromal cells (HESCs) and minimally decreases the production of Ang-2 protein in human endometrial endothelial cells (HEECs). Hence the presence of thrombin due to aberrant bleeding could affect the angiogenic potential of the endometrium, creating a feed forward loop resulting in more thrombin, weak vasculature, and more bleeding. In addition, since the exact localization of Ang in the human endometrium remains a subject of controversy, we have addressed this issue in an in vivo system by analyzing the expression of Angs by microdissection of HESCs, HEECs, and human endometrial glandular epithelial cells followed by real time, quantitative RT-PCR.

ACCESSION NUMBER: 2004262436 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15161644
TITLE: Endometrial angiopoietin expression and modulation by thrombin and steroid hormones: a mechanism for abnormal angiogenesis following long-term progestin-only contraception.
AUTHOR: Krikun Graciela; Sakkas Denny; Schatz Frederick; Buchwalder Lynn; Hylton Donna; Tang Caroline; Lockwood Charles J
CORPORATE SOURCE: Department of Obstetrics, Yale University, School of Medicine, New Haven, Connecticut 06520-8063, USA.. graciela.krikun@yale.edu
CONTRACT NUMBER: R01 HD33937-06 (NICHD)
SOURCE: The American journal of pathology, (2004 Jun) Vol. 164, No. 6, pp. 2101-7.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 27 May 2004
Last Updated on STN: 9 Jul 2004
Entered Medline: 8 Jul 2004

L1 ANSWER 7 OF 14 MEDLINE on STN

TI Evaluation of the antiangiogenic effect of Taxol in a human epithelial ovarian carcinoma cell line.

AB PURPOSE: Angiopoietin-1 (Ang-1) and angiopoietin-2 (Ang-2) are major ligands for the endothelium-specific tyrosine kinase receptor Tie-2 and are important regulators of endothelial cell survival. In the presence of vascular endothelial growth factor (VEGF), vessel destabilization by Ang-2 has been hypothesized to induce an angiogenic response, but in the absence of VEGF, Ang-2 leads to vessel regression. In the present study, a human ovarian cancer cell line was used to investigate the possibility that Taxol might affect the expression of Ang-1, Ang-2, and VEGF. MATERIALS AND METHODS: KF 28, a single-cell clone of a human ovarian epithelial carcinoma cell line, was used. The expression of Ang-1, Ang-2, and VEGF was assessed by quantitative real-time RT-PCR and Western blot analysis or enzyme-linked immunosorbent assay. Conditioned medium was used in the in vitro angiogenesis assay. RESULTS: The concentration of Taxol that inhibited the growth of cells to the level of 50% of control cell growth was 4.65+/-0.35 nM. Quantitative real-time RT-PCR indicated that Ang-1

gene expression was significantly decreased by exposure to 2 nM Taxol for 168 h (P<0.05 vs control cells). Western blot analysis confirmed that the Ang-1 protein level was decreased by exposure to 2 nM Taxol for 168 h. Ang-2 gene expression did not significantly differ between control cells and those exposed to Taxol for any of the indicated times. The Ang-1/ Ang-2 gene expression ratio was significantly decreased by exposure to Taxol for 168 h (P<0.05 vs control cells). VEGF gene expression was significantly decreased by exposure to Taxol for 168 h (P<0.05). The VEGF concentration in the conditioned medium was also significantly reduced by exposure to Taxol for 168 h (P<0.05). Conditioned medium collected following Taxol treatment for 168 h significantly inhibited endothelial tubule formation (P<0.05). Cell growth did not significantly differ between control cells and those exposed to Taxol for any of the indicated times. CONCLUSIONS: Our results show that exposure of ovarian cancer cells to a low concentration of Taxol may inhibit the initiating event in angiogenesis, namely, vascular regression. This information might be valuable in the development of new therapeutic interventions for epithelial ovarian cancer.

ACCESSION NUMBER: 2003576581 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14569416
TITLE: Evaluation of the antiangiogenic effect of Taxol in a human epithelial ovarian carcinoma cell line.
AUTHOR: Hata Kohkichi; Osaki Mitsuhiko; Dhar Dipok Kumar; Nakayama Kentaro; Fujiwaki Ritsuto; Ito Hisao; Nagasue Naofumi; Miyazaki Kohji
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Shimane Medical University, 693-8501, Izumo, Japan.. hata31@med.shimane-u.ac.jp
SOURCE: Cancer chemotherapy and pharmacology, (2004 Jan) Vol. 53, No. 1, pp. 68-74. Electronic Publication: 2003-10-21. Journal code: 7806519. ISSN: 0344-5704.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 4 Feb 2004
Entered Medline: 3 Feb 2004

L1 ANSWER 8 OF 14 MEDLINE on STN
TI Localized expression of angiopoietin 1 and 2 may explain unique characteristics of the rat testicular microvasculature.
AB The testicular vasculature is unique in several ways. The unfenestrated endothelial cells constitute one part of the blood-testis barrier, and testicular microvessels are normally resistant to inflammation mediators. At the same time that angiogenic factors and inflammation mediators are constitutively produced, the proportion of proliferating endothelial cells is considerably higher than in other organs, but new blood vessels are not formed. Hormonal stimulation of the testis with hCG increase endothelial cell proliferation, vascular permeability, and sensitivity to locally injected inflammation mediators. In the present study, we examined whether local expression of angiopoietin (ang) 1, an inhibitor of vascular leakage and sprouting angiogenesis, and its antagonist, ang 2, could be involved in establishing this vascular phenotype. Using reverse transcription-polymerase chain reaction and immunohistochemistry, we demonstrate that testicular vascular endothelial growth factor-A (VEGF-A), ang 1, ang 2, and the ang-receptor tie 2 are expressed in the testis and that hormonal stimulation with hCG is accompanied by increased expression of VEGF-A and ang 2. The ang 1 protein is expressed in testicular microvessels under basal conditions, and it is largely unaffected after hCG stimulation. Expression of ang 2 in microvessels, in contrast, is low under basal conditions and is

up-regulated by hCG. Intratesticular injection of human recombinant ang 1 protein inhibits hCG-induced increase in vascular permeability. Injection of ang 2 in the testis increases endothelial cell proliferation and the volume of the interstitial space. We therefore suggest that ang 1 stabilizes testicular microvessels under basal conditions and that a shift in this balance caused by increased ang 2, together with increased VEGF-A, allows vascular leakage, high endothelial cell proliferation, and presumably, vascular growth after hormonal stimulation.

ACCESSION NUMBER: 2003439539 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12773423
TITLE: Localized expression of angiopoietin 1 and 2 may explain unique characteristics of the rat testicular microvasculature.
AUTHOR: Haggstrom Rudolfsson Stina; Johansson Anna; Franck Lissbrant Ingela; Wikstrom Pernilla; Bergh Anders
CORPORATE SOURCE: Department of Surgical and Perioperative Sciences, Urology and Andrology, Umea University, Sweden.
SOURCE: Biology of reproduction, (2003 Oct) Vol. 69, No. 4, pp. 1231-7. Electronic Publication: 2003-05-28. Journal code: 0207224. ISSN: 0006-3363.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 23 Sep 2003
Last Updated on STN: 18 Dec 2003
Entered Medline: 11 Dec 2003

L1 ANSWER 9 OF 14 MEDLINE on STN
TI A quantitative gene expression study suggests a role for angiopoietins in focal nodular hyperplasia.
AB BACKGROUND AND AIMS: Although the pathogenesis of focal nodular hyperplasia (FNH) of the liver remains unclear, a vascular mechanism has been suspected. To gain insight into the pathogenesis of FNH, we performed a large-scale quantitative study of gene expression in FNH. METHODS: Quantitative expression level of 209 selected genes was assessed using real-time reverse-transcription polymerase chain reaction in 14 cases of FNH and compared with their expression level in 13 cases of liver cirrhosis, 4 adenomas, and 15 hepatocellular carcinomas. RESULTS: Among the 7 genes, the expression of which was significantly up-regulated or down-regulated in FNH, the most informative markers for the diagnosis of FNH as assessed using the receiving operative curve and area under the curve (AUC) were angiopoietin-1 (Ang-1; AUC, 0.82) and angiopoietin-2 (Ang-2; AUC, 0.80). These 2 genes are involved in the regulation of vasculogenesis. In FNH, Ang-1 was significantly up-regulated, Ang-2 was down-regulated, and the Ang-1/Ang-2 ratio was highly and specifically increased in FNH compared with normal liver or other groups of lesions (FNH, 15.2-fold increase; HCC, 2.78; adenoma, 2.28; cirrhosis, 1.92; $P < 0.01$ for FNH vs. all groups, analysis of variance). Tie-2 messenger RNA, the receptor of Ang-1 and Ang-2, was detected at the same level in FNH as in normal liver. Ang-1 protein was detected on Western blot of FNH and expressed by endothelial cells of dystrophic vessels and sinusoids as shown by immunohistochemistry. CONCLUSIONS: A specific increase of Ang-1/Ang-2 ratio in FNH, in the presence of the functional Tie-2 receptor, might be involved in the formation of hyperplastic and dystrophic vessels of FNH.

ACCESSION NUMBER: 2003109093 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12612904
TITLE: A quantitative gene expression study suggests a role for angiopoietins in focal nodular hyperplasia.
AUTHOR: Paradis Valerie; Bieche Ivan; Dargere Delphine; Laurendeau

Ingrid; Nectoux Juliette; Degott Claude; Belghiti Jacques; Vidaud Michel; Bedossa Pierre

CORPORATE SOURCE: Service d'Anatomie Pathologique and Service de Chirurgie, Hopital Beaujon, Clichy, France.. vparadis@teaser.fr

SOURCE: Gastroenterology, (2003 Mar) Vol. 124, No. 3, pp. 651-9.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 8 Mar 2003
Last Updated on STN: 28 Mar 2003
Entered Medline: 27 Mar 2003

L1 ANSWER 10 OF 14 MEDLINE on STN

TI Angiopoietin-1 is expressed in the synovium of patients with rheumatoid arthritis and is induced by tumour necrosis factor alpha.

AB OBJECTIVES: To examine the potential role of the angiogenic growth factor angiopoietin-1 (Ang-1) in inflammatory arthritis. METHODS: Eighteen synovial tissue samples were obtained from 17 patients with a clinical diagnosis of rheumatoid arthritis (RA) and compared with six synovial tissue samples from six patients with osteoarthritis (OA). Ang-1 expression in synovial tissues was determined by immunohistochemistry and in situ hybridisation. Ang-1 mRNA and protein expression were also examined by northern blot analysis and enzyme linked immunosorbent assay (ELISA) in cultured synovial fibroblasts and human umbilical vein endothelial cells (HUVECs) before and after treatment with tumour necrosis factor (TNF)alpha. RESULTS: Ang-1 protein expression was detected by immunohistochemistry in 16/18 RA synovial tissue samples. Ang-1 protein was frequently observed in the synovial lining layer and in cells within the sublining synovial tissue, in both perivascular areas and in areas remote from vessels. In contrast, Ang-1 was only weakly detected in these sites in OA samples. Ang-1 mRNA and protein were also expressed in cultured synovial fibroblasts derived from patients with RA. In addition, induction of Ang-1 mRNA and protein was observed by northern blot analysis and ELISA after stimulation of RA synovial fibroblasts, but not HUVECs, with the proinflammatory cytokine TNF alpha. CONCLUSIONS: Ang-1 mRNA and protein are expressed in the synovium of patients with RA, and are up regulated in synovial fibroblasts by TNF alpha. Ang-1 may therefore be an important regulator of angiogenesis in inflammatory arthritis.

ACCESSION NUMBER: 2003018719 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12525377

TITLE: Angiopoietin-1 is expressed in the synovium of patients with rheumatoid arthritis and is induced by tumour necrosis factor alpha.

AUTHOR: Gravallese E M; Pettit A R; Lee R; Madore R; Manning C; Tsay A; Gaspar J; Goldring M B; Goldring S R; Oettgen P

CORPORATE SOURCE: Beth Israel Deaconess Medical Center, Department of Medicine, New England Baptist Bone and Joint Institute, Harvard Institutes of Medicine, 4 Blackfan Circle, Boston, MA 02115, USA.

CONTRACT NUMBER: R01-HL63008 (NHLBI)
SOURCE: Annals of the rheumatic diseases, (2003 Feb) Vol. 62, No. 2, pp. 100-7.
Journal code: 0372355. ISSN: 0003-4967.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 15 Jan 2003
Last Updated on STN: 4 Mar 2003
Entered Medline: 3 Mar 2003

L1 ANSWER 11 OF 14 MEDLINE on STN

TI Abnormal uterine bleeding during progestin-only contraception may result from free radical-induced alterations in angiopoietin expression.

AB Abnormal uterine bleeding is the leading indication for discontinuation of long-term progestin-only contraceptives (LTPOCs). Histological sections of endometria from LTPOC-treated patients display abnormally enlarged blood vessels at bleeding sites. Paradoxically, a trend toward reduced endometrial perfusion in LTPOC users has been reported in these patients. We hypothesized that hypoxia/reperfusion-induced free radical production inhibits the expression of angiopoietin-1 (Ang-1), a vessel stabilizing factor, leaving unopposed the effects of endothelial Ang-2, a vessel-branching and permeability factor. Immunohistochemical studies confirmed selective decreases in stromal cell Ang-1 in LTPOC-exposed endometrium. To indirectly assess whether LTPOC enhances endometrial free radical production, immunostaining was conducted for the phosphorylated form of the stress-activated kinases SAPK/JNK and p38. These kinases were greatly increased in endometria from LTPOC-treated patients. Interestingly, the endothelial cells but not the stromal cells displayed enhanced immunostaining for the phosphorylated mitogen-activated kinase (pMAPK) after LTPOC treatment. To further examine the effects of progestin, hypoxia, and reactive oxygen species (ROS) on the regulation of Ang-1 and Ang-2 as well as the activation of MAPK, SAPK/JNK, and p38 by the relevant cell types, we conducted in vitro studies with cultured human endometrial stromal cells (HESCs) and human endometrial endothelial cells (HEECs). Cultures of HESCs were treated with vehicle control, estradiol (E(2)), or with medroxyprogesterone acetate +/- E(2) under hypoxic and normoxic conditions. Although medroxyprogesterone acetate but not E(2) increased Ang-1 expression, hypoxia greatly decreased Ang-1 protein and mRNA expression. In contrast, HESCs did not appear to express Ang-2 protein or mRNA. Conversely, cultured HEECs did not appear to express Ang-1, but expressed Ang-2, the levels of which were significantly increased by hypoxia. Hypoxia also induced the phosphorylation of SAPK/JNK and p38 in both cultured HESCs and HEECs. Moreover, ROS such as that observed after hypoxia/reperfusion resulted in the activation of SAPK/JNK and p38 in HESCs and HEECs and inhibited Ang-1 in cultured HESCs. These effects could be blocked by oxygen radical scavengers. Consistent with the in vivo studies, MAPK was activated after ROS treatment in HEECs but not in HESCs. Our findings suggest that LTPOC-induced endometrial bleeding occurs as a result of hypoxia/reperfusion-induced free radicals that directly damage vessels and alter the balance of Ang-1 and Ang-2 to produce the characteristic enlarged and permeable vessels that are prone to bleeding.

ACCESSION NUMBER: 2002454846 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12213726
TITLE: Abnormal uterine bleeding during progestin-only contraception may result from free radical-induced alterations in angiopoietin expression.
AUTHOR: Krikun Graciela; Critchley Hilary; Schatz Frederick; Wan Livia; Caze Rebeca; Baergen Rebecca N; Lockwood Charles J
CORPORATE SOURCE: Department of Obstetrics and Gynecology, New York University Medical Center, New York, USA..
graciela.krikun@yale.edu
CONTRACT NUMBER: R01 HD33937-06 (NICHD)
SOURCE: The American journal of pathology, (2002 Sep) Vol. 161, No. 3, pp. 979-86.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 6 Sep 2002
Last Updated on STN: 28 Sep 2002
Entered Medline: 27 Sep 2002

L1 ANSWER 12 OF 14 MEDLINE on STN
TI Angiopoietin-1 and VEGF in vascular development and angiogenesis in hypoplastic lungs.
AB We hypothesized that exposure of murine fetuses to environmental toxins, such as nitrofen, during early embryogenesis alters vasculogenesis. To address our hypothesis, we assessed protein levels of endothelial cell-selective angiogenic factors: angiopoietin (ANG)-1, vascular endothelial growth factor (VEGF), and mediator of VEGF signaling, VEGF receptor-2 [fetal liver kinase (Flk)-1], a transmembrane receptor tyrosine kinase. VEGF and Flk-1 proteins were lower in hypoplastic lungs from pseudoglandular to alveolar stages than in normal lungs at equivalent developmental time points significant for induction of pulmonary vasculogenesis and angiogenesis. ANG-1 protein was higher in hypoplastic lungs than in normal lungs at all the developmental stages considered in this study, i.e., pseudoglandular, canalicular, saccular, and alveolar stages. We assessed exogenous VEGF-mediated endothelial cell response on extracellular signal-regulated kinase (ERK) 1/2, also referred to as p44/42 mitogen-activated protein kinase. Hypoplastic lungs had more elevated ERK 1/2 protein than normal developing lungs. Exposure to exogenous VEGF activated ERK 1/2 in normal developing lungs but not in hypoplastic lungs. Our results suggest that in hypoplastic lungs: 1) low VEGF signifies negative effects on vasculogenesis/angiogenesis and indicates altered endothelial-mesenchymal interactions; 2) increased ANG-1 protein may be required to maintain vessel integrity and quiescence; and 3) regulation of ERK 1/2 protein is affected in hypoplastic lungs. We speculate that extensive remodeling of blood vessels in hypoplastic lungs may occur to compensate for structurally and functionally defective vasculature.
ACCESSION NUMBER: 2002317153 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12060561
TITLE: Angiopoietin-1 and VEGF in vascular development and angiogenesis in hypoplastic lungs.
AUTHOR: Chinoy Mala R; Graybill Megan M; Miller Shane A; Lang C Max; Kauffman Gordon L
CORPORATE SOURCE: Lung Development Research Program, Department of Surgery, Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033, USA.. mchinoy@psu.edu
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2002 Jul) Vol. 283, No. 1, pp. L60-6. Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 13 Jun 2002
Last Updated on STN: 20 Jul 2002
Entered Medline: 19 Jul 2002

L1 ANSWER 13 OF 14 MEDLINE on STN
TI Increased renal angiopoietin-1 expression in folic acid-induced nephrotoxicity in mice.
AB Growth factors affect epithelial regeneration after acute renal injury, but less is known regarding the expression of vascular growth factors in this setting. A mouse model of folic acid (FA)-induced nephrotoxicity was

used to study the expression of angiopoietins (Ang), factors that bind the Tie-2 receptor and modulate endothelial growth. Tubular damage was detected 1 d after FA administration; in the next 14 d, most tubules regenerated but patchy atrophy, with interstitial fibrosis, was also observed. Ang-1 immunostaining was detected between cortical tubules and in the vasa rectae of vehicle-treated animals. FA-induced nephropathy was associated with the acquisition of Ang-1 immunostaining in renal arterial walls and in a subset of injured cortical tubules that failed to stain with periodic acid-Schiff stain, which indicated that they were distal tubules. Renal Ang-1 protein levels were significantly increased after FA administration, compared with time-matched control values, as assessed by Western blotting. Capillaries between regenerating tubules expressed both Tie-2 and platelet-endothelial cell adhesion molecule. A subset of these endothelia expressed proliferating cell nuclear antigen, whereas capillary proliferation was absent in control samples. Therefore, FA-induced nephropathy is associated with increased Ang-1 protein expression in renal epithelia and arteries. In addition, Tie-2-expressing capillaries near damaged cortical tubules undergo proliferation. Further experiments are required to establish whether these events are functionally related.

ACCESSION NUMBER: 2001682132 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11729241
TITLE: Increased renal angiopoietin-1 expression in folic acid-induced nephrotoxicity in mice.
AUTHOR: Long D A; Woolf A S; Suda T; Yuan H T
CORPORATE SOURCE: Nephro-Urology Unit, Institute of Child Health, University College London, London, United Kingdom.
SOURCE: Journal of the American Society of Nephrology : JASN, (2001 Dec) Vol. 12, No. 12, pp. 2721-31.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 3 Dec 2001
Last Updated on STN: 13 Feb 2002
Entered Medline: 12 Feb 2002

L1 ANSWER 14 OF 14 MEDLINE on STN
TI The 3T3-L1 fibroblast to adipocyte conversion is accompanied by increased expression of angiopoietin-1, a ligand for tie2.
AB The tie2 receptor tyrosine kinase plays a key role in angiogenesis, and the remodeling and maturation of blood vessels. In this study we have used a factor-dependent cell line (Ba/F3) expressing a chimeric receptor containing the extracellular domain of mouse tie2 and the transmembrane and cytoplasmic domain of the erythropoietin receptor to identify specific binding activity associated with an adipogenic sub-line of 3T3 fibroblasts (3T3-L1). 3T3-L1 fibroblasts are capable of undergoing differentiation to adipocytes under specific culture conditions. When compared to 3T3-L1 cells, the adipocyte differentiated cultures, which contain both pre-adipocytes and adipocytes, exhibited a significantly increased ability to support the growth of Ba/F3 cells expressing the chimeric receptor. Using probes specific for two recently described ligands for tie2, Ang-1 and Ang-2, we have shown that mRNA encoding Ang-1 is upregulated when 3T3-L1 fibroblasts are differentiated to adipocytes. These results suggest that the levels of Ang-1 protein and mRNA in 3T3-L1 cells can be regulated by cellular differentiation in adipose development.

ACCESSION NUMBER: 2001238892 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11334054
TITLE: The 3T3-L1 fibroblast to adipocyte conversion is

accompanied by increased expression of angiopoietin-1, a ligand for tie2.

AUTHOR: Stacker S A; Runting A S; Caesar C; Vitali A; Lackmann M; Chang J; Ward L; Wilks A F

CORPORATE SOURCE: Ludwig Institute for Cancer Research, Royal Melbourne Hospital, Victoria, Australia..
Steven.stacker@ludwig.edu.au

SOURCE: Growth factors (Chur, Switzerland), (2000) Vol. 18, No. 3, pp. 177-91.
Journal code: 9000468. ISSN: 0897-7194.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200109

ENTRY DATE: Entered STN: 24 Sep 2001
Last Updated on STN: 11 Dec 2002
Entered Medline: 20 Sep 2001